

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

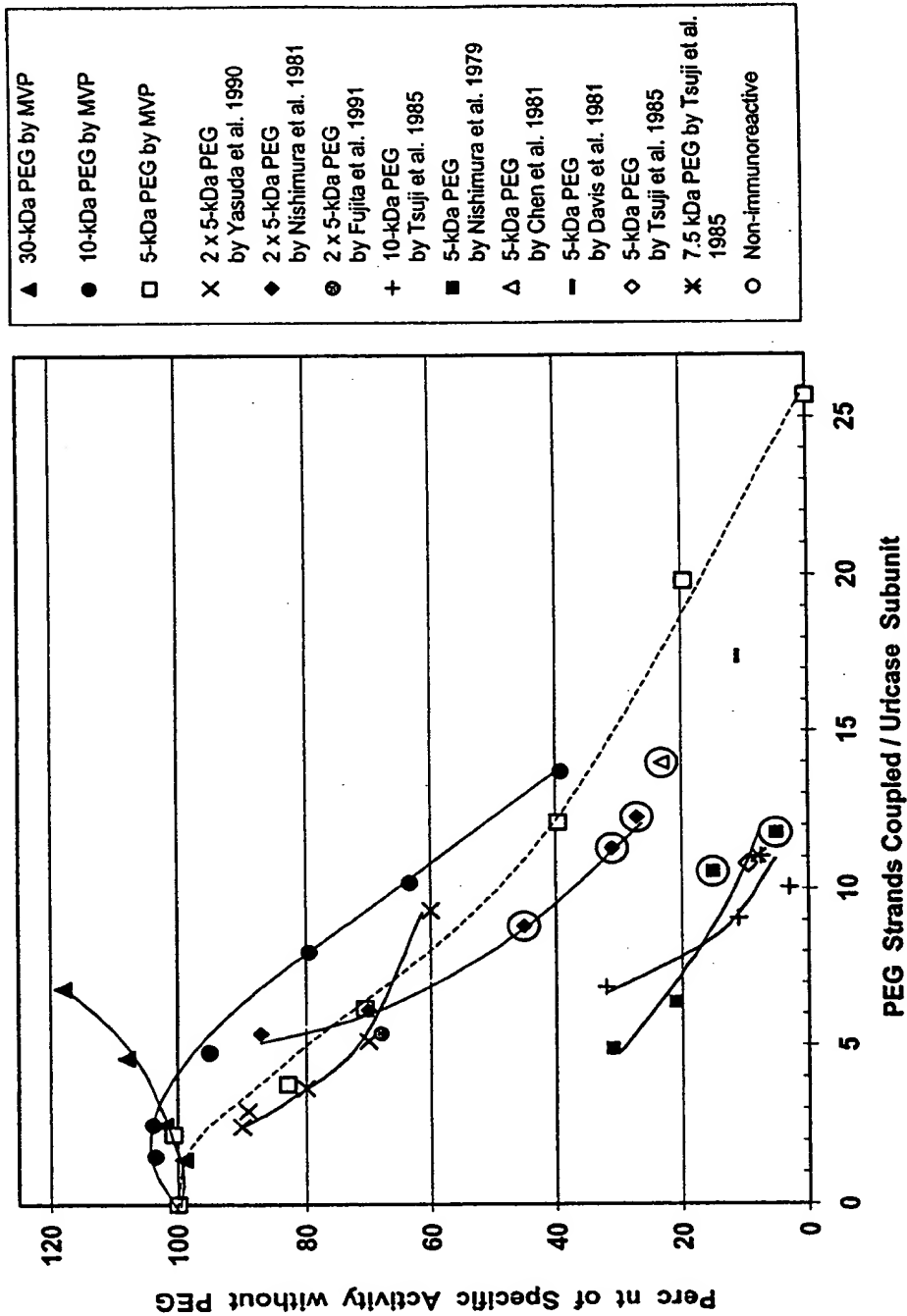
Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.

**Figure 1A: Retention of Activity by PEGylated *Candida* Uricase**



**Figure 1B: Retention of Activity by PEGylated Candida Uricase**

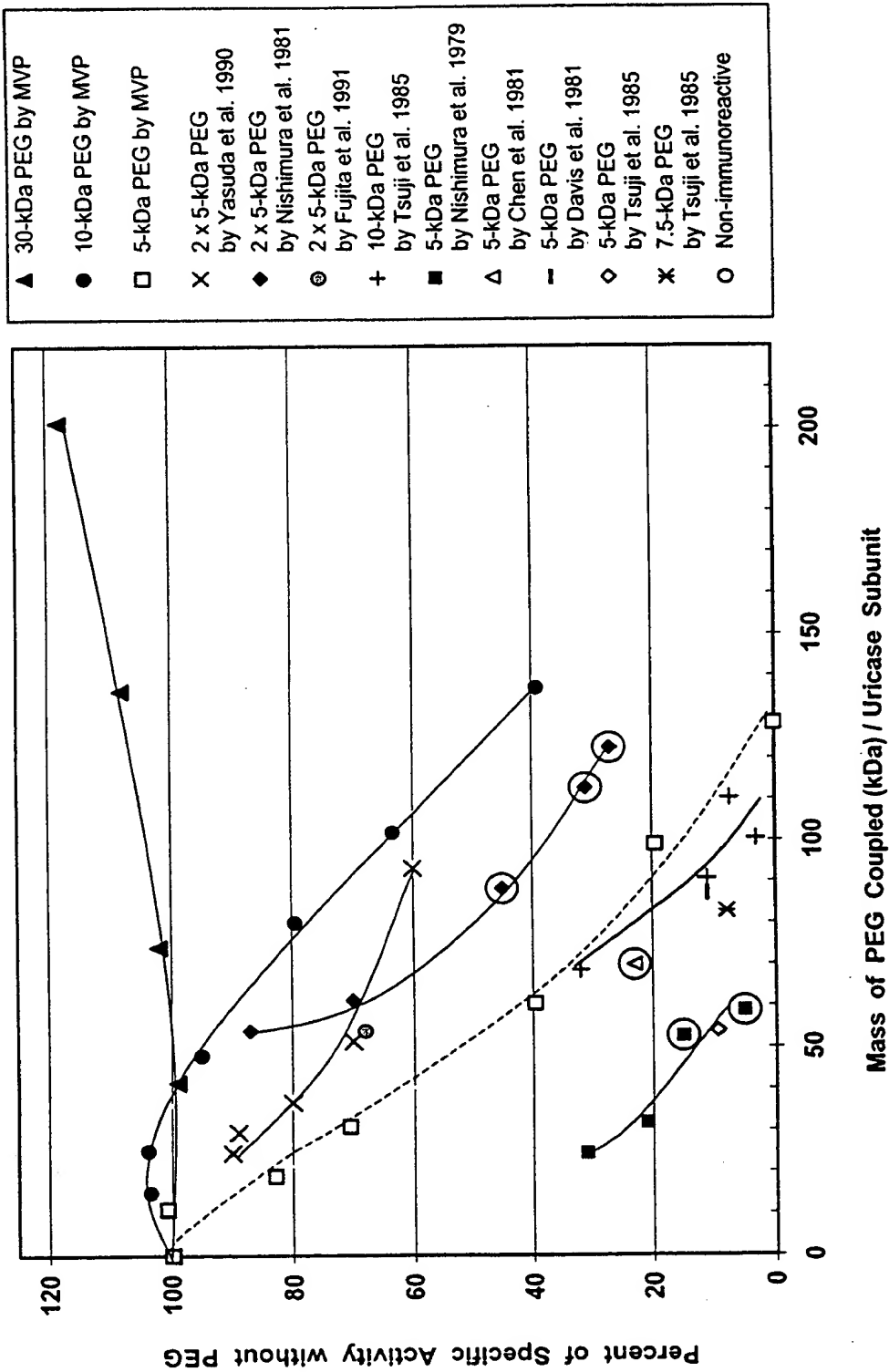


Figure 2A: Retention of Activity by PEGylated Porcine Uricase

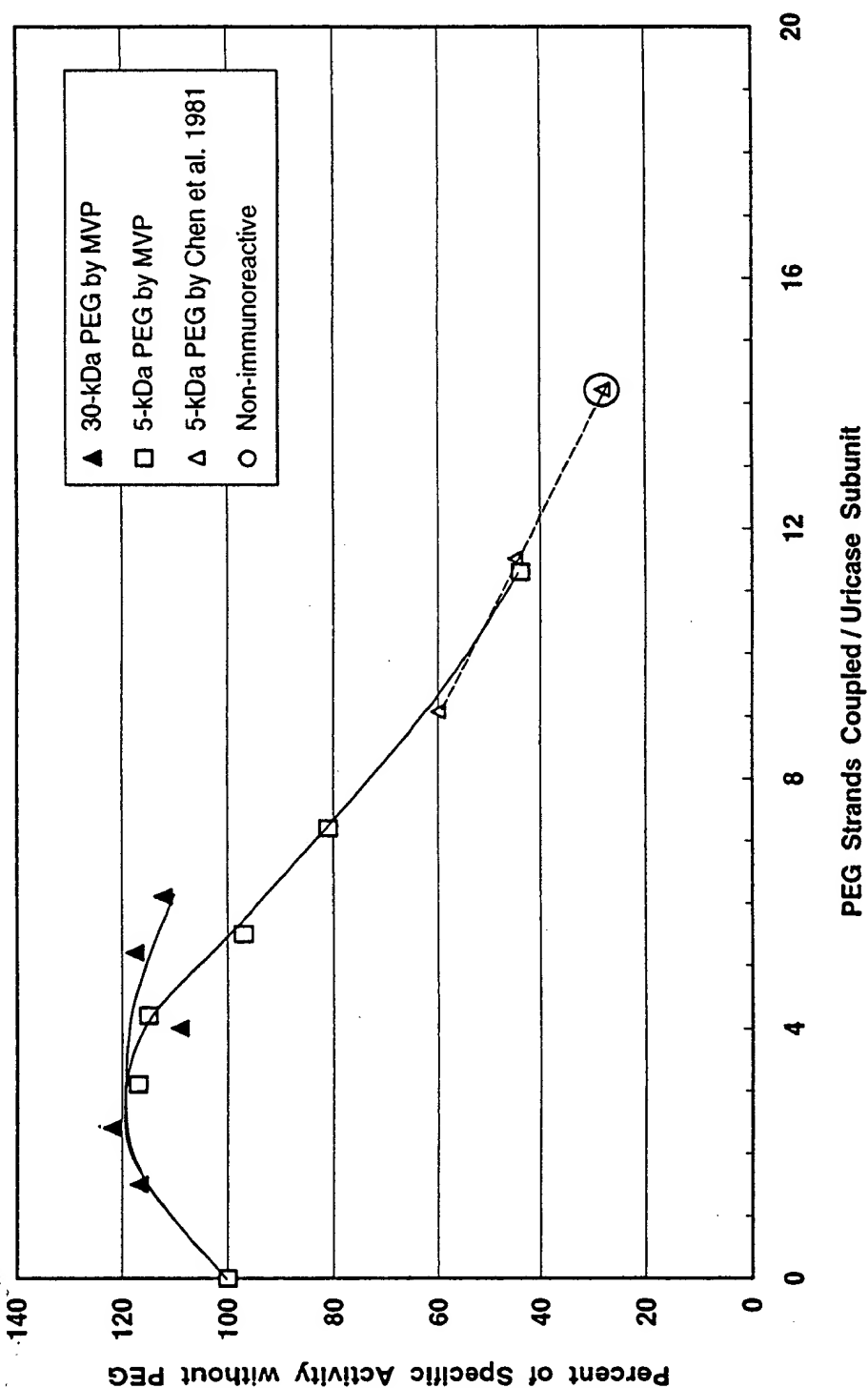


Figure 2B: Retention of Activity by PEGylated Porcine Uricase

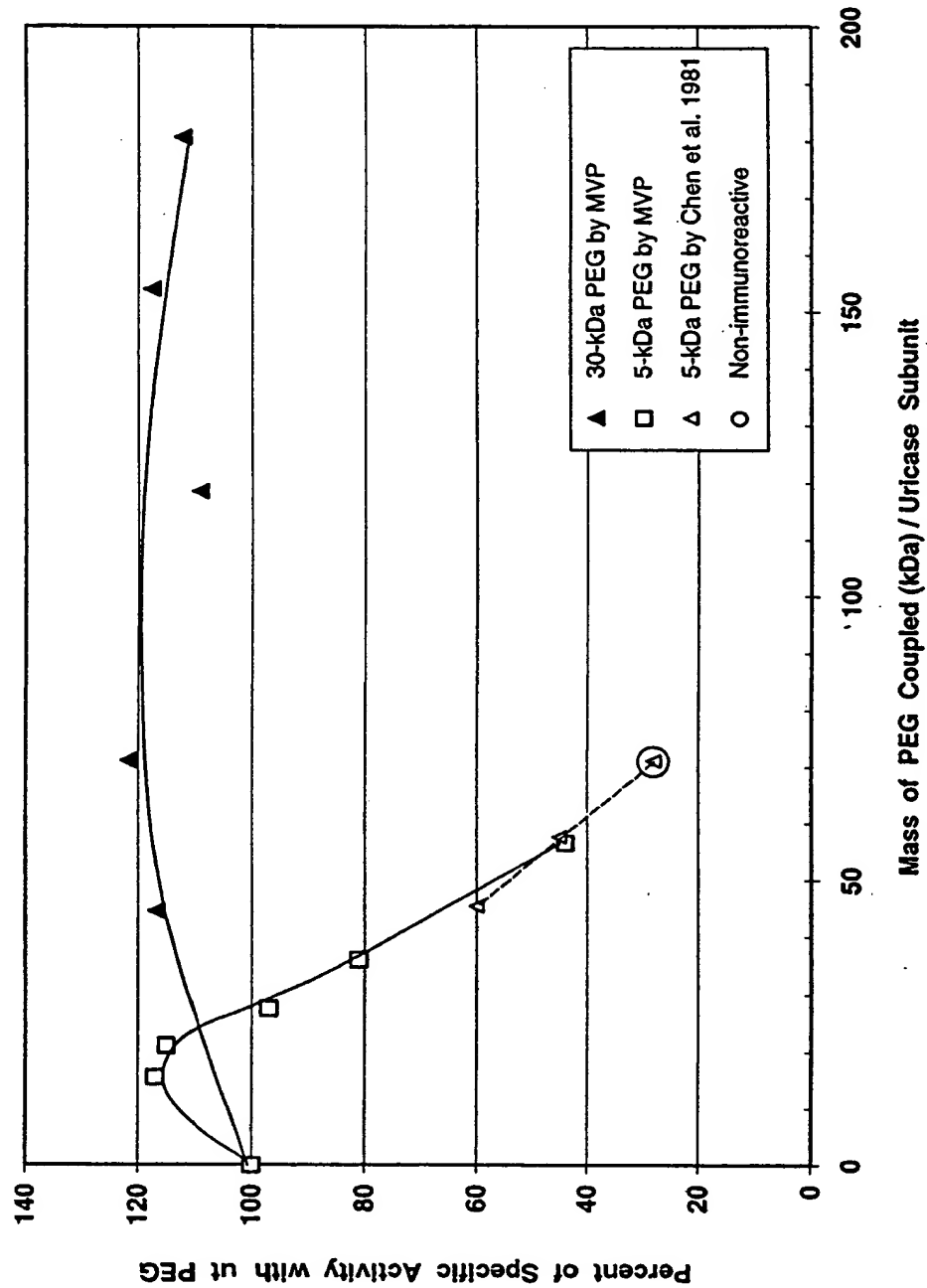


Figure 3A: Retention of Activity by PEGylated PBC Uricase

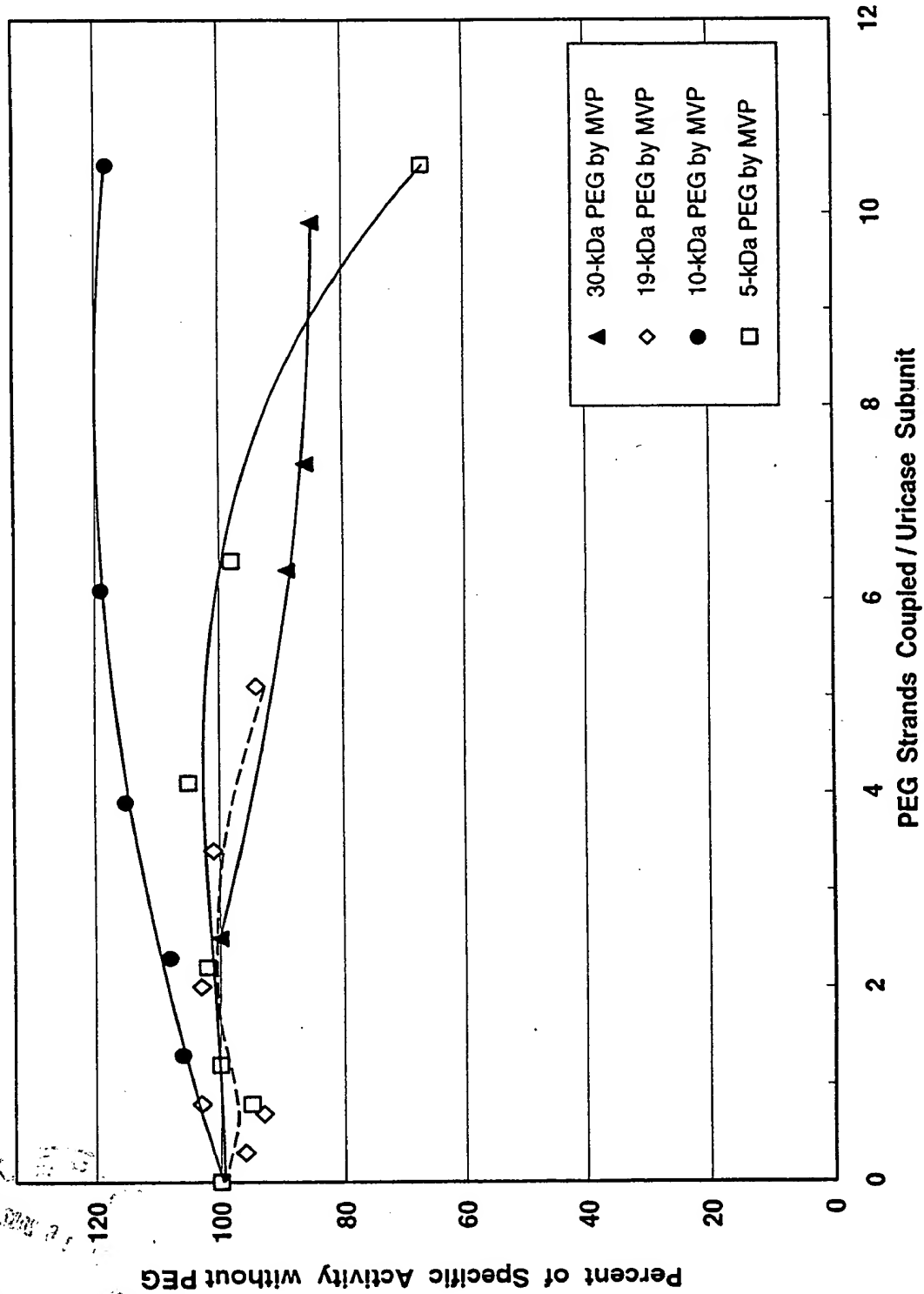


Figure 3B: Retention of Activity by PEGylated PBC Uricase

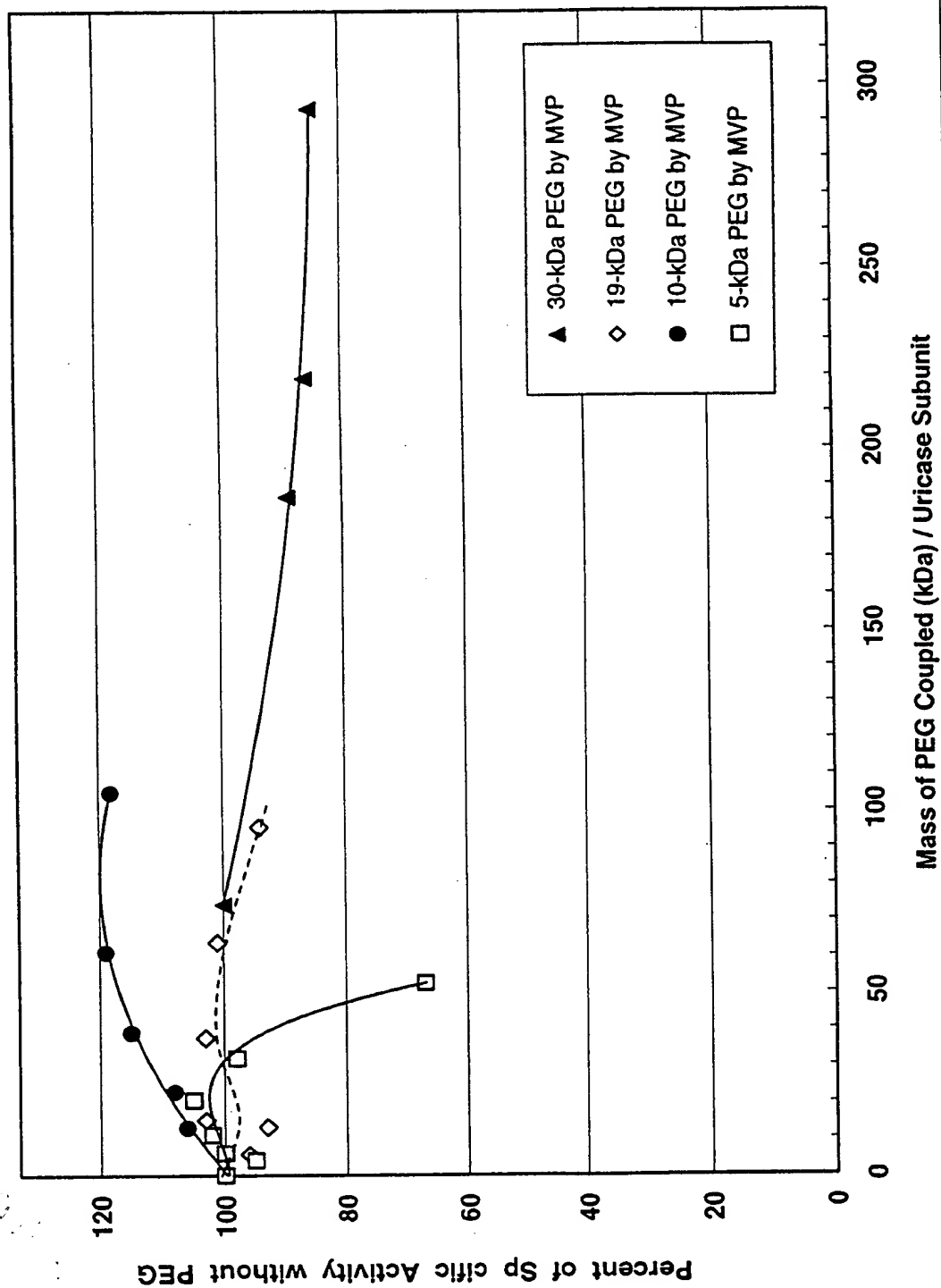
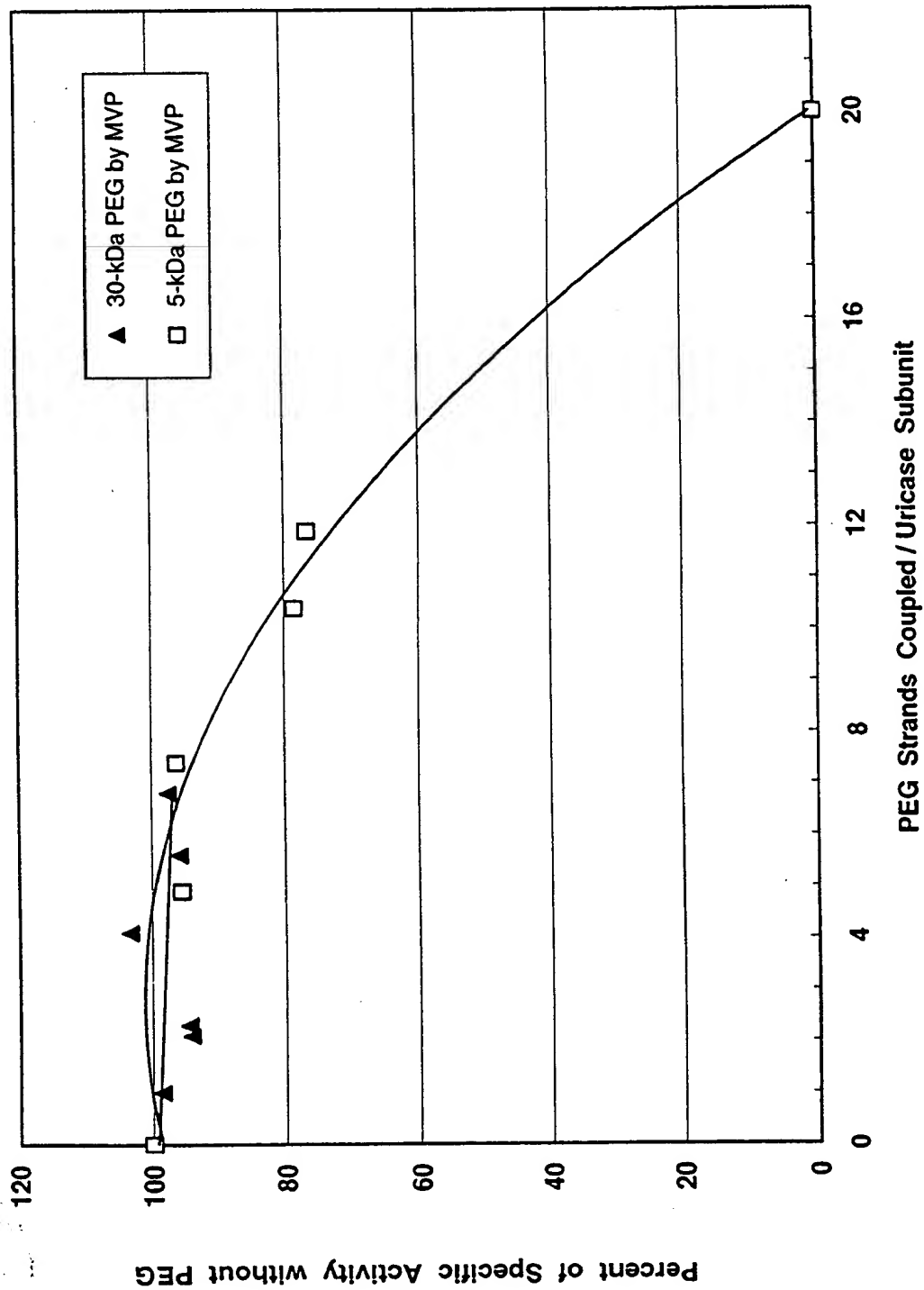


Figure 4A:  
Retention of Activity by PEGylated Uricozyme® (*A. flavus* Uricase)





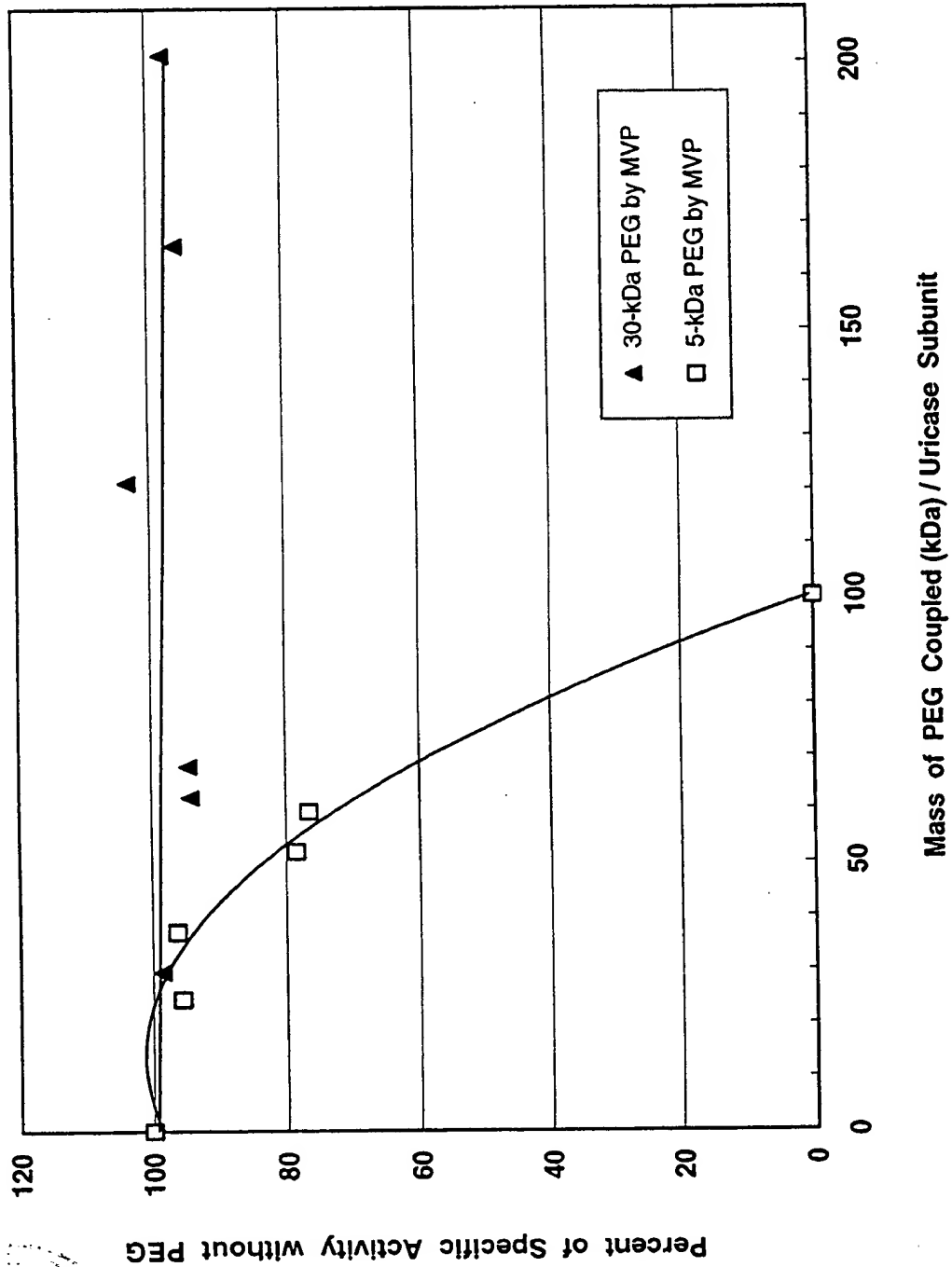
## URATE OXIDASE CONJUGATES AND USE THE

Williams, et al.

Appl. No.: 09/839946

Atty Docket: MVIEWD.1A2DV1

Figure 4B:  
Retention of Activity by PEGylated Uricozyme® (*A. flavus* Uricase)



-URATE OXIDASE CONJUGATES AND USE THEREOF  
Williams, et al.

Appl. No.: 09/839946

Atty Docket: MVIEWD.1A2DVI

Figure 5A: Retention of Activity by PEGylated Soybean Uricase

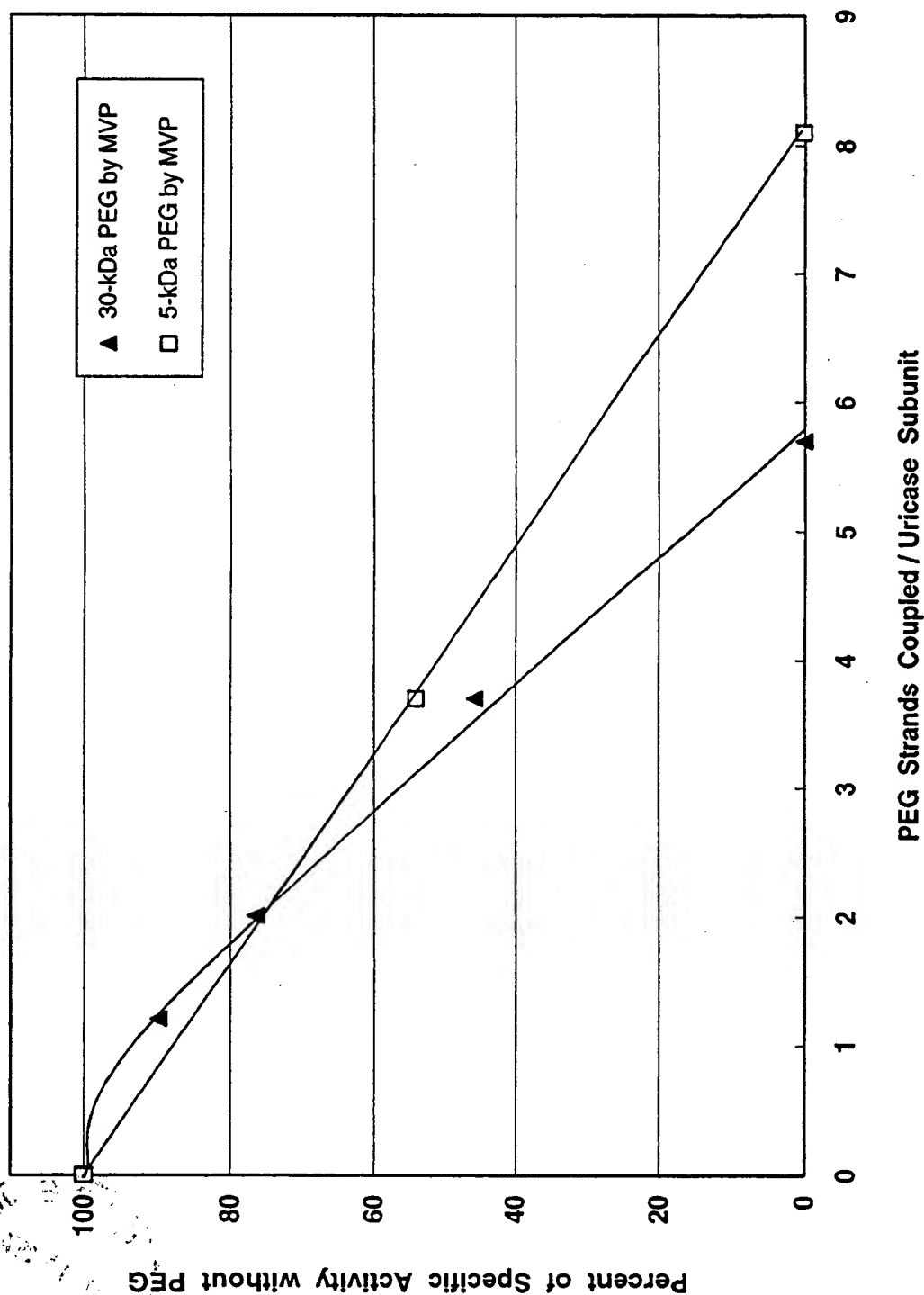
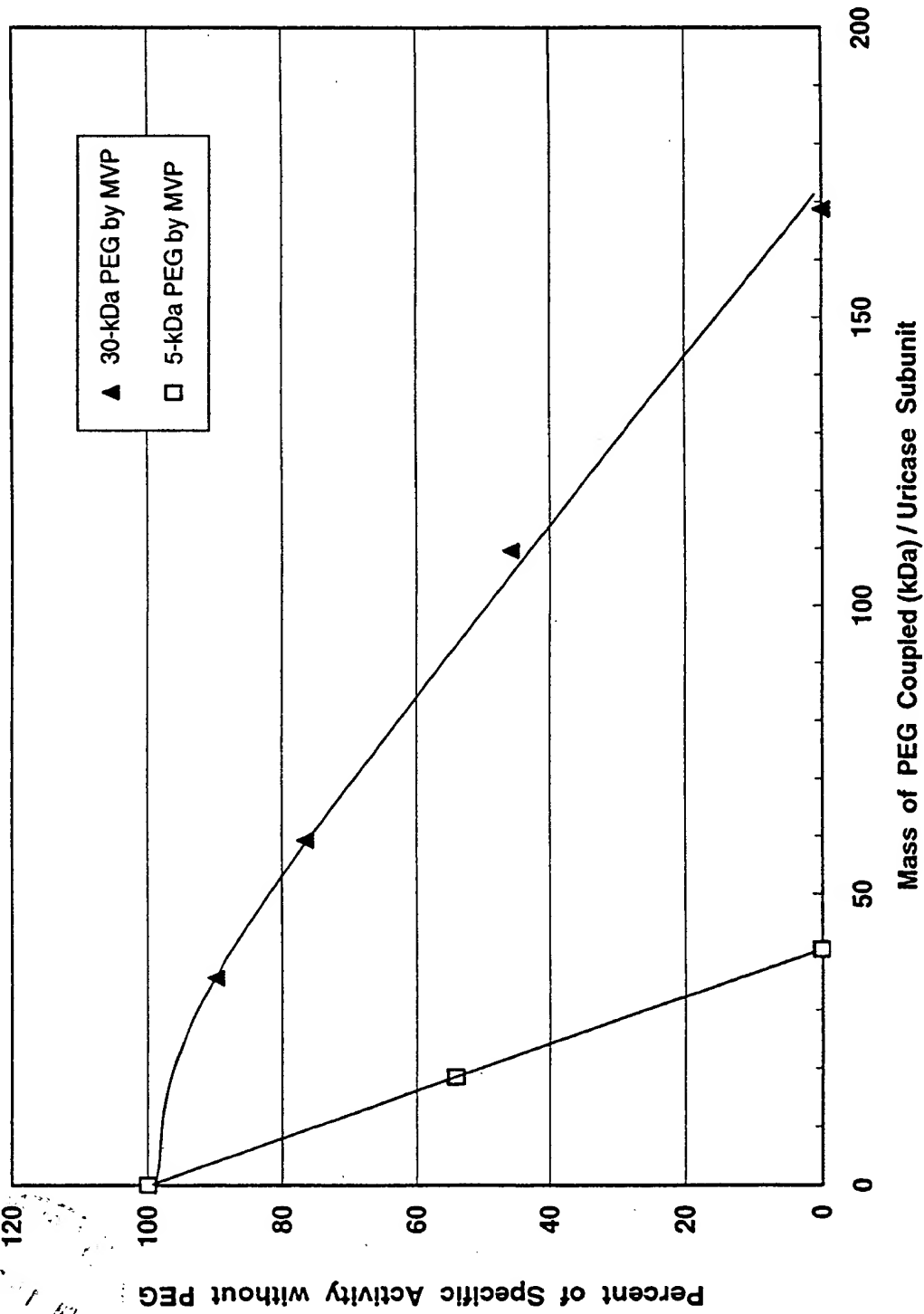


Figure 5B: Retention of Activity by PEGylated Soybean Uricase



## PURATE OXIDASE CONJUGATES AND USE THERE

Williams, et al.

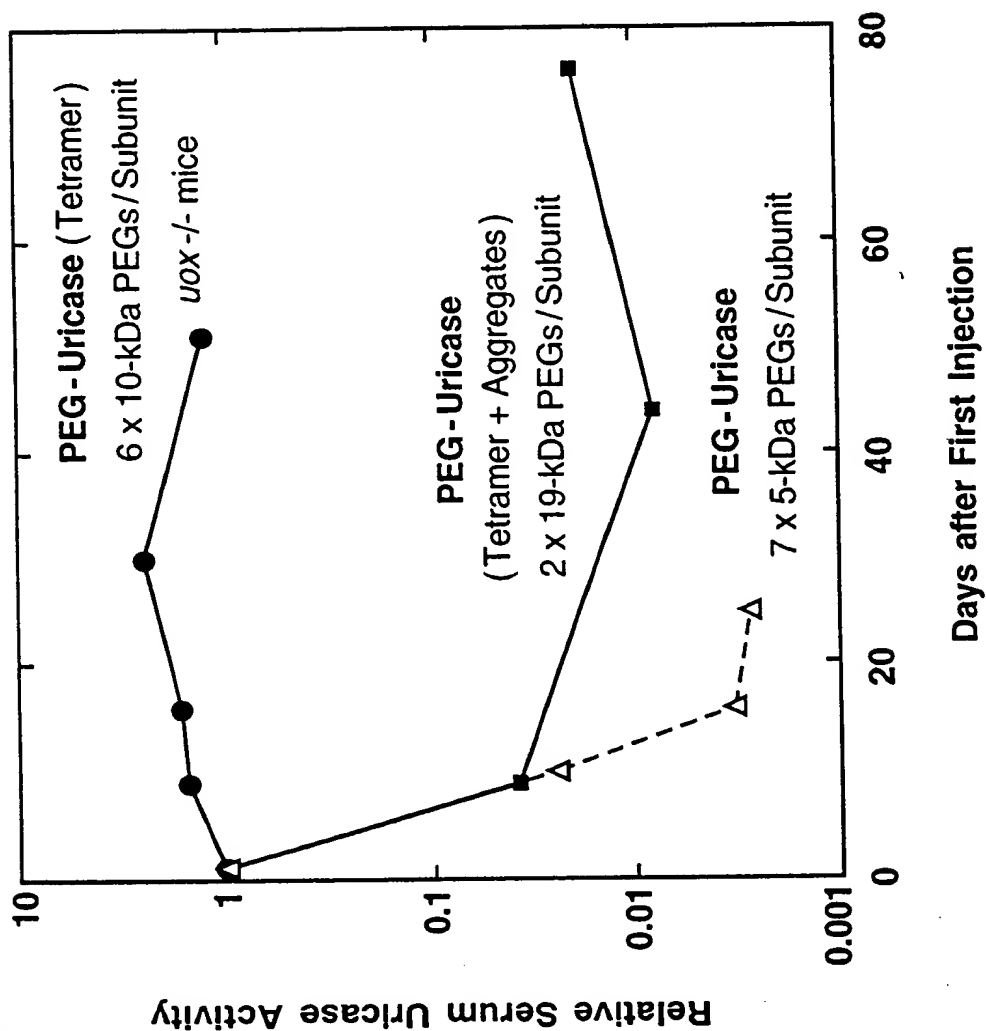
Appl. No.: 09/839946

Atty Docket: MVIEWD.1A2DV1

Figure 6: Deduced amino acid sequences of Pig-Baboon Chimeric (PBC) uricase, PBC uricase that is truncated at the amino and carboxyl terminals (PBC-NT-CT) and Porcine uricase containing the mutations R291K and T301S (PKS Uricase) (SEQ ID NO:3), compared with the porcine sequence (SEQ ID NO: 1) and baboon sequence (SEQ ID NO: 2)

|           |                                             |     |
|-----------|---------------------------------------------|-----|
| Porcine   | MAHYRNDYKK NDEVEFVRTG YGKDMIKVLH IQRDGKYHSI | 40  |
| PBC       | porcine sequence 1-225 →                    | 40  |
| PBC-NT-CT | porcine sequence 1-219 →                    | 34  |
| PKS       | porcine sequence 1-288 →                    | 40  |
| Baboon    | MADYHNNYKK NDELEFVRTG YGKDMVKVLH IQRDGKYHSI | 40  |
| Porcine   | KEVATSVQLT LSSKKDYLHG DNSDVIPTDT IKNTVNVLAK | 80  |
| PBC       | porcine sequence →                          | 80  |
| PBC-NT-CT | porcine sequence →                          | 74  |
| PKS       | porcine sequence →                          | 80  |
| Baboon    | KEVATSVQLT LSSKKDYLHG DNSDIPTDT IKNTVHVLAKE | 80  |
| Porcine   | FKGIKSIETF AVTICEHFLS SFKHVIRAQV YVEEVPWKRF | 120 |
| PBC       | porcine sequence →                          | 120 |
| PBC-NT-CT | porcine sequence →                          | 114 |
| PKS       | porcine sequence →                          | 120 |
| Baboon    | FKGIKSIEAF GVNICEYFLS SFNHVIRAQV YVEEIPWKRL | 120 |
| Porcine   | EKNGVKHVHA FIYTPTGTHF CEVEQIRNGP PVIHSGIKDL | 160 |
| PBC       | porcine sequence →                          | 160 |
| PBC-NT-CT | porcine sequence →                          | 154 |
| PKS       | porcine sequence →                          | 160 |
| Baboon    | EKNGVKHVHA FIHTPTGTHF CEVEQLRSGP PVIHSGIKDL | 160 |
| Porcine   | KVLKTTQSGF EGFIKDQFTT LPEVKDRCFA TQVYCKWRYH | 200 |
| PBC       | porcine sequence →                          | 200 |
| PBC-NT-CT | porcine sequence →                          | 194 |
| PKS       | porcine sequence →                          | 200 |
| Baboon    | KVLKTTQSGF EGFIKDQFTT LPEVKDRCFA TQVYCKWRYH | 200 |
| Porcine   | QGRDVFDEAT WDTVRSIVLQ KFAGPYDKGE YSPSVQKTLY | 240 |
| PBC       | porcine sequence →   ← baboon sequence      | 240 |
| PBC-NT-CT | porcine sequence →   ← baboon sequence      | 234 |
| PKS       | porcine sequence →                          | 240 |
| Baboon    | QCRDVFDEAT WGTIRDLVLE KFAGPYDKGE YSPSVQKTLY | 240 |
| Porcine   | DIQVLTGQV PEIEDMEISL PNIHYLNIDM SKMGLINKEE  | 280 |
| PBC       | baboon sequence →                           | 280 |
| PBC-NT-CT | baboon sequence →                           | 274 |
| PKS       | porcine sequence →                          | 280 |
| Baboon    | DIQVLSLSRV PEIEDMEISL PNIHYFNIDM SKMGLINKEE | 280 |
| Porcine   | VLLPLDNPYG RITGTVKRKL TSRL                  | 304 |
| PBC       | baboon sequence →                           | 304 |
| PBC-NT-CT | baboon sequence →                           | 295 |
| PKS       | porcine   ← baboon →                        | 304 |
| Baboon    | VLLPLDNPYG KITGTVKRKL SSRL                  | 304 |

Figure 7: Serum Uricase Activity 24 Hours after Each  
PEG-Uricase Injection, Relative to the First Injection



PEG-URICASE OXIDASE CONJUGATES AND USE THEREOF

Williams, et al.

Appl. No. 09/839946

Atty Docket: MVIEWD.1A2DV1

Figure 8: Inverse Relationship between Serum PEG-Uricase Activity and Uric Acid Levels in the Serum and Urine of a Uricase-Deficient Mouse

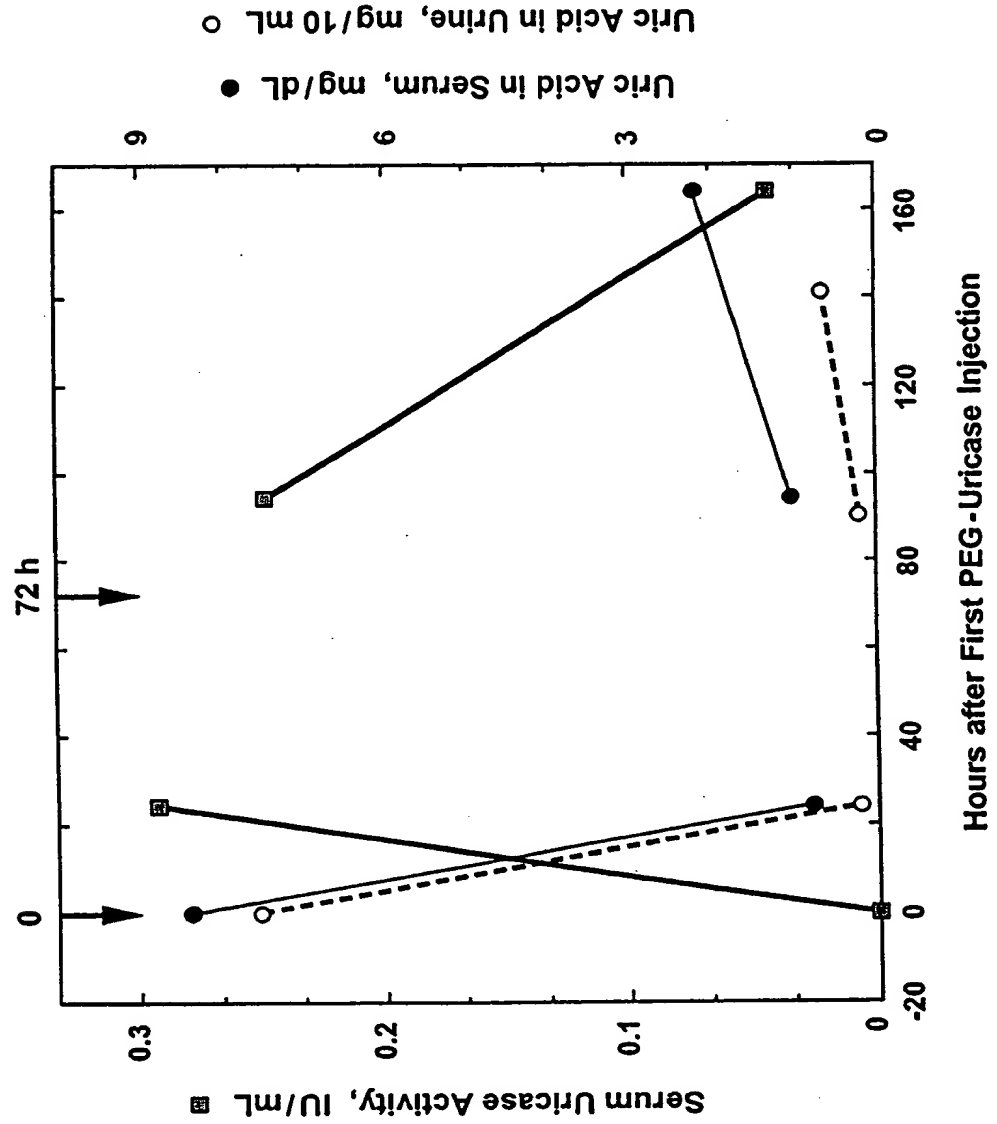


Figure 9: Decreased Severity of Urine-Concentrating Defect  
in Uricase-Deficient Mice Treated with PEG-Uricase

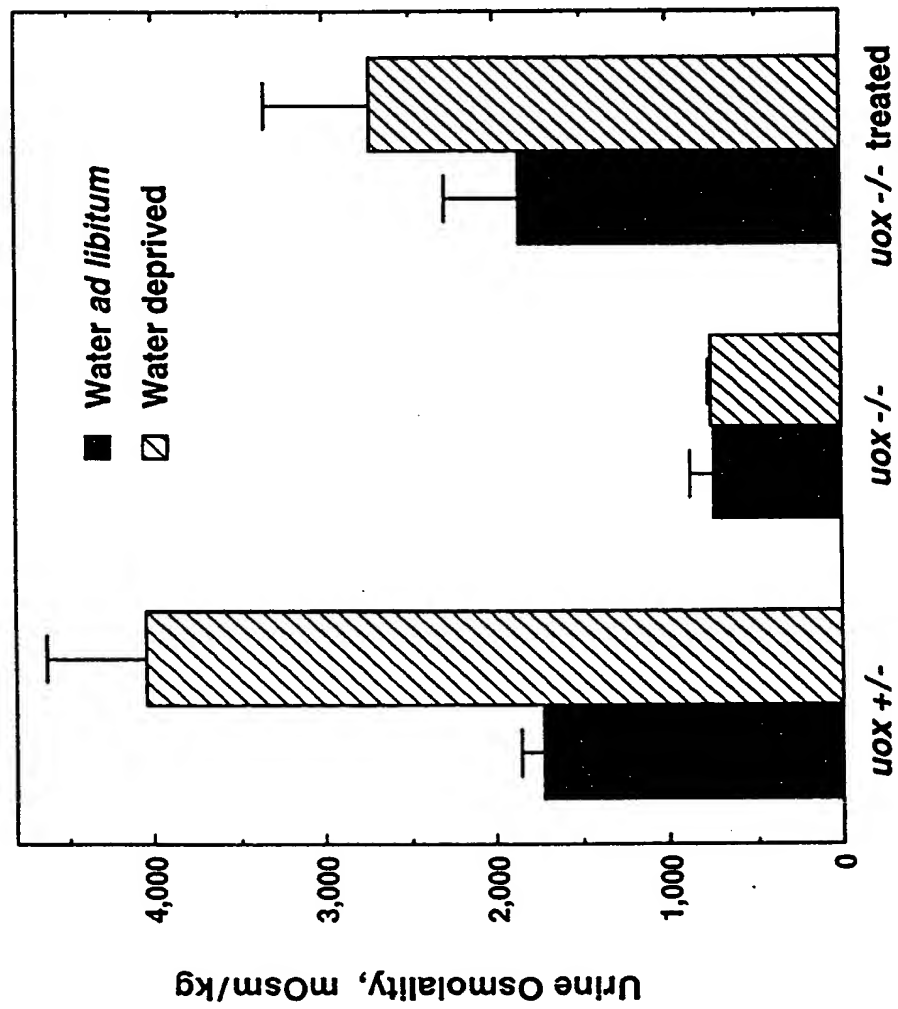


Figure 10: Decreased Severity of Nephrogenic Diabetes Insipidus  
in Uricase-Deficient Mice Treated with PEG-Uricase

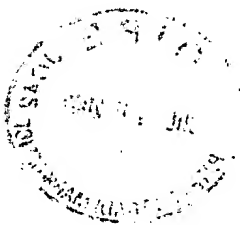
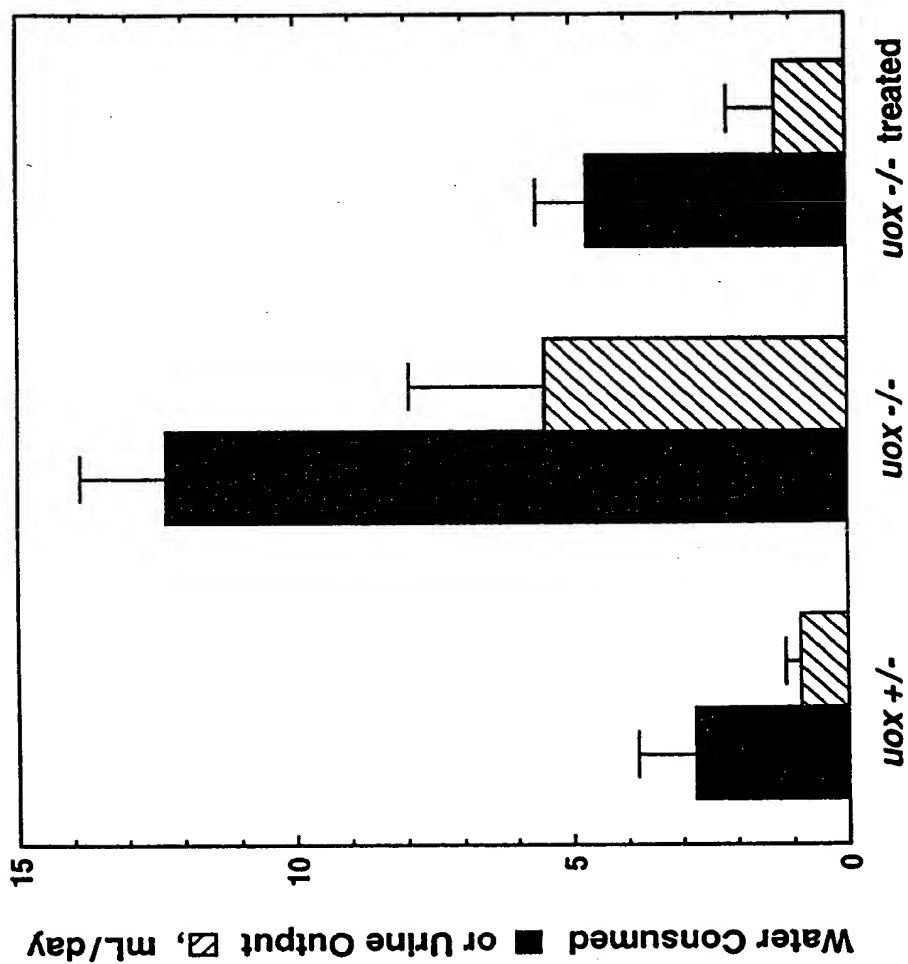




Figure 11:

Decreased Severity of Uric Acid-Induced Nephropathy after Treatment with PEG-Uricase, as Visualized by Magnetic Resonance Microscopy

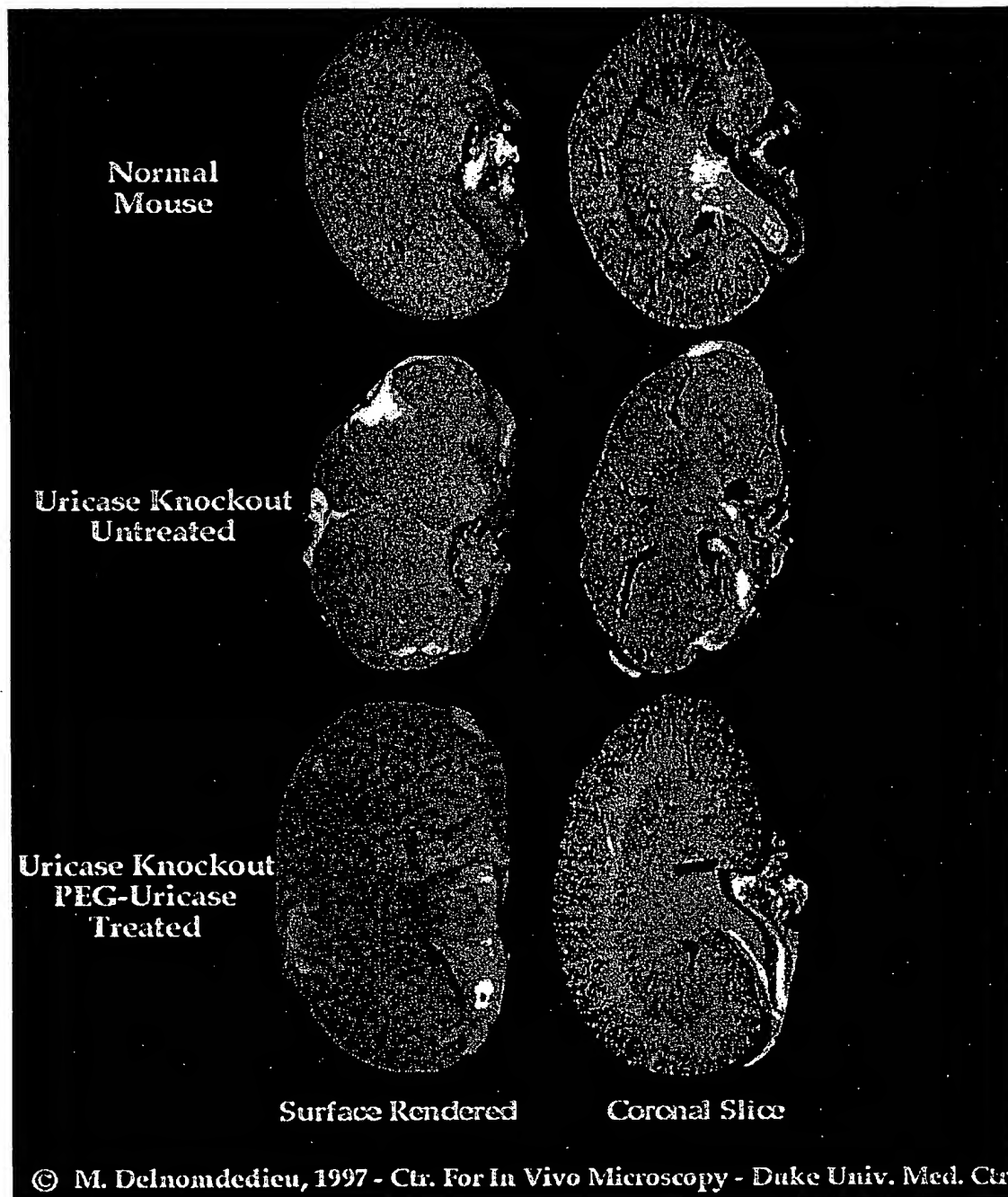


Figure 12: Clearance from the Circulation of BALB/c Mice of PBC Uricase Tetramer and Octamer Coupled to 5-6 Strands of 10-kDa PEG/Subunit

